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A randomized, 6-wk trial of a low FODMAP diet in patients with inflammatory bowel disease

Giorgia Bodini M.D., Ph.D. *, Claudia Zanella BS.c, Mattia Crespi M.D., Sara Lo Pumo M.D., Maria Giulia Demarzo M.D., Edoardo Savarino M.D., Ph.D., Vincenzo Savarino M.D., Edoardo G. Giannini M.D., Ph.D.

Gastroenterology Unit, Department of Internal Medicine, University of Genoa, Ospedale Policlinico San Martino-IRCCS per l'Oncologia, Genoa, Italy

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ABSTRACT

Objective: The aim of this study was to assess the safety and efficacy of a low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAP) diet (LFD) in patients with inflammatory bowel disease (IBD).
Methods: An LFD is associated with symptom improvement in patients with functional intestinal disorders, although its safety and efficacy has not been characterized in patients with IBD. Fifty-five patients with IBD in remission or with mild disease activity were randomized to a 6-wk LFD or standard diet (SD). Disease activity (Harvey–Bradshaw index [HBi], partial Mayo score), fecal calprotectin, and disease-specific quality of life (IBD-Q) were assessed at baseline and at the end of dietary intervention.
Results: After the 6-wk dietary intervention, median HBi decreased in the LFD (4; IQR, 3–5 versus 3; IQR, 2–3; $P = 0.024$) but not in the SD (3; IQR, 3–3 versus 3; IQR, 2–4), whereas Mayo scores were numerically decreased in the LFD group and unmodified in the SD group. Median calprotectin decreased in the LFD (76.6 mg/kg; IQR, 50–286.3 versus 50 mg/kg; IQR, 50.6–81; $P = 0.004$) but not in the SD group (91 mg/kg; IQR, 50.6–143.6 versus 87 mg/kg; IQR, 50–235.6). Lastly, we observed a barely significant increase in median IBD-Q in the LFD group (166; IQR, 139–182 versus 177; IQR, 155–188; $P = 0.05$) and no modification in the SD group (181; IQR, 153–197 versus 166; IQR, 153–200).
Conclusions: A short-term, LFD is safe for patients with IBD, and is associated with an amelioration of fecal inflammatory markers and quality of life even in patients with mainly quiescent disease.

Introduction

Inflammatory bowel diseases (IBD) are idiopathic autoimmune conditions that include Crohn's disease (CD) and ulcerative colitis (UC) [1]. The therapeutic armamentarium available to treat IBD has consistently expanded in recent years, and now includes, in addition to immunosuppressants such as azathioprine and methotrexate, biologic drugs such as infliximab, adalimumab, vedolizumab, and golimumab [2–5]. The principal goal of treatment is to induce remission of disease, clinical, biochemical, and endoscopic. In many patients with IBD, actual disease remission may not be accompanied by a complete resolution of symptoms, as patients in remission or with minimal disease activity often present some troublesome gastrointestinal (GI) symptoms that may be related to the presence of concurrent functional disturbances, such as irritable bowel syndrome (IBS) [6,7]. As a fact, IBS-like symptoms tend to be overrepresented even in patients with quiescent IBD, and IBS has a higher prevalence in patients with IBD than in the general population [8,9]. These symptoms may trigger an unnecessary overtreatment that can be harmful, and their presence may have a detrimental effect on patient quality of life (QoL), which is a particularly relevant issue in patients with a chronic condition such as IBD [6,7,9].

Due to the absence of an available, effective treatment for IBS and to the fact that the majority of patients with IBS tend to correlate their symptoms to food ingestion, dietary management has been proposed as an appealing, potential therapeutic approach for this condition [10–15]. The use of a diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) also has been proposed as a therapeutic option in patients with IBD [13,16–21]. FODMAPs consist of molecules that are

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* Corresponding author: Tel./Fax: +39 010 3538956.
E-mail address: giorgia.bodini@unige.it (G. Bodini).

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poorly absorbed in the small intestine and are fermented by bacteria in the colon, and as such may elicit symptoms in patients with IBD that is in remission or with minimal disease activity [17,18]. Indeed, a diet low in FODMAPs proved to be able to improve some symptoms (i.e., abdominal pain, bloating, diarrhea) in a retrospective study based on phone interviews where IBD activity was not assessed, and in a review of medical records of patients with IBD who were referred for dietary advice, although in a randomized, placebo-controlled, crossover, rechallenge trial only fructans restriction seemed to provide symptomatic improvement [16–18,20]. Lastly, a recent meta-analysis confirmed the beneficial effect on symptoms of a low FODMAP diet (LFD) in patients with IBD, thus calling for further well-designed and prospective studies to confirm this finding [21]. Nevertheless, possible drawbacks of an LFD in patients with IBD also have been reported as, theoretically, such a diet may reduce substrates that have a beneficial effect on colonic epithelial cells. However, studies addressing the potential for a detrimental effect on disease activity are lacking [22].

In this prospective study, our aim was to assess the effect and safety of an LFD by assessing clinical and biochemical disease activity, as well as QoL, in patients with IBD after a 6-wk nutritional plan; patients were managed by a team of clinicians and nutritionists who monitored both the disease activity and the need for modification in drug treatment throughout the entire study period.

Patients and methods

Patients

In this prospective study, we enrolled patients with IBD who were in the remission phase or who had mild disease activity, as assessed by a Mayo score <6 in patients with UC and a Harvey–Bradshaw Index (HBi) <8 in patients with CD, who were followed at our institution. Inclusion criteria for this study were as follows: men and women between 18 and 80 y of age; diagnosis of IBD (confirmed by endoscopic, radiologic, and histologic evaluation); presence of functional GI symptoms that met Roma IV criteria for the diagnosis of IBS; and stable IBD therapy with no modification of treatment (i.e., mesalazine, azathioprine, methotrexate, or biologic therapy) within at least the 12-wk period before enrollment [23]. Exclusion criteria were the presence of moderate to severe disease; previous, extensive GI surgery or stenotic disease; presence of diet-related disorders or diseases with potential influence of diet manipulation (i.e., celiac disease, lactose intolerance, diabetes, chronic kidney disease), and a preexisting dietetic program.

Therefore, from an initial cohort of 127 patients with IBD, we enrolled 60 who fulfilled the inclusion criteria and who had no exclusion criteria for the study. Briefly, 67 patients were not included in the study for the following reasons: 38 had moderate to severe disease, 2 had concurrent celiac disease, 13 were already on a spontaneous diet therapy, and 14 refused to participate in the study. Among the 60 patients with IBD who agreed to participate in the study, after explanation of the dietary intervention, 2 patients were not included due to a worsening of bowel disease that required treatment modification before diet initiation, 2 felt the diet too restrictive in relation to their lifestyle, and 1 decided to withdraw the informed consent before the beginning of the diet (Fig. 1). Thus, 55 patients (35 patients with CD, 20 patients with UC) were available for our investigation and represented the final population that was randomized to receive an LFM or a standard diet (SD). In this cohort, the majority of patients were treated with mesalazine (n = 27, 49.1%), 21 patients (38.2%) were on immunosuppressive therapy (12 on anti-TNF drugs [21.8%] and 9 on azathioprine [16.4%]), and 7 patients had no treatment (12.7%).

Methods

All individuals who agreed to participate in our investigation underwent careful history taking, physical, clinical, and nutritional examination (including current medication, height and weight recording, tobacco use, alcohol and coffee consumption, and food history). Body mass index (BMI) was calculated for all patients, and according to BMI, patients were categorized as underweight (<25 kg/m^2), normal weight (25–28 kg/m^2), overweight (28–30 kg/m^2), and obese (>30 kg/m^2).

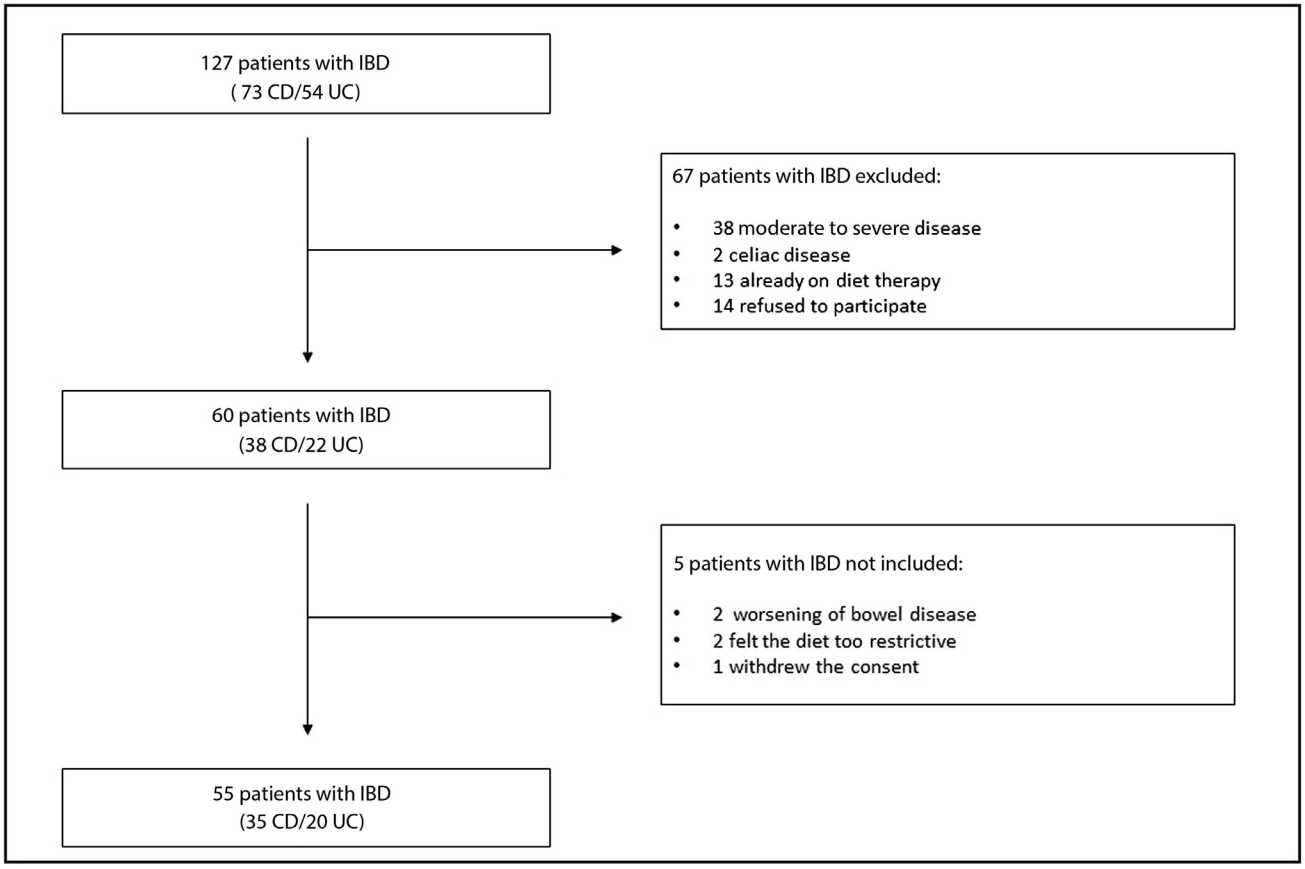

Fig. 1. Patient flow and disposition within the study. CD, Crohn's disease; IBD, inflammatory bowel disease; UC, ulcerative colitis.

At the first visit (T_0), patients were evaluated by both a gastroenterologist and a dietitian: All patients underwent complete blood examination, including C-reactive protein (CRP) levels, and assessment of fecal calprotectin (Quantum Blue fCAL, Buhlmann). Briefly, the Buhlmann Quantum Blue fCAL relies on the established lateral flow technology, where optical densities of test and control lines are detected by the reader and translated into a quantitative result. This assay uses a highly specific monoclonal antibodies method to capture the calprotectin molecule, and is used as a point-of-care test. The sensitivity of the test is 30μg/g, and the dynamic range is 30 to 1000 μg/g. The Montreal classification was used to assess IBD location and behavior in patients with CD [24]. IBD activity was defined using the partial Mayo score and the HBi for patients with UC and CD, respectively. At the same visit, all patients were asked to complete a scientifically validated, disease-specific questionnaire on QoL (IBD-Q). The IBD-Q is a 32-item questionnaire consisting of four dimensions: bowel-related symptoms (i.e., loose stools, abdominal pain), systemic function (i.e., fatigue, sleep pattern), social function (i.e., ability to attend work and social events), and emotional status (i.e., anger, depression, irritability) [25]. The response for each question ranges from 1 to 7, with 1 corresponding to *significant impairment* and 7 corresponding to *no impairment*. The IBD-Q score is the sum of the responses to each question. Total IBD-Q score can range from 32 (*very poor health-related quality of life* [HRQoL]) to 224 (*perfect HRQoL*). Patients in symptomatic remission usually have a score >170 [25].

After initial assessment, patients were randomized using a free computerized program (www.randomizer.org) to two different diets: either an LFD) or an SD containing a usual FODMAP amount. The diets were specifically studied by an expert dietitian with expertise in the LFD and all patients received a 30- to 45-min consultation to explain the assigned diet. All patients were encouraged to eat three main meals (breakfast, lunch, and dinner with different types and amounts of food), and to consume two snacks during the day. At every main meal, the dietitian gave patients the possibility to choose at least three different types of menus. All menus were characterized by the same caloric and FODMAP amount. Moreover, patients were provided with explanatory leaflets regarding meal preparation and a food diary was used to assess patient adherence to the various diets. Nutritional supplements were not permitted.

During the 6-wk dietary intervention, a dedicated e-mail address, monitored by the clinician in charge of the study who was blinded regarding the type of diet assigned to the patients, was provided to the patients so as to receive potential messages regarding modifications in disease status. Compliance with the diet was assessed by the dedicated dietitian by means of weekly phone calls. Moreover, a food diary was recorded daily by the patients with almost 90% accuracy. Only two patients, one in the LFD group and one in the SD group did not achieve 90% accuracy compiling the diary (83% and 87%, respectively). After the 6-wk dietary intervention (T_1), patients had a second visit with the same gastroenterologist and dietitian, and underwent complete blood examination workup, including CRP levels, fecal calprotectin evaluation, anthropometric data measurement, and were again administered the IBD-Q.

The study was performed according to the Declaration of Helsinki. All patients were asked to provide written informed consent before the start of the study.

Statistical analysis

Continuous data are presented as median and interquartile range (IQR), whereas categorical data are presented as absolute value and percentage. Categorical variables were compared using the Fisher's exact test. The Wilcoxon's test for paired data was used to assess clinical and biochemical disease activity indexes and IBD-Q modifications within groups at the beginning (T_0) and at the end (T_1) of the dietary intervention. The Mann–Whitney U test was used for the comparison between groups. Study data were evaluated in an intent-to-treat analysis. $P < 0.05$ in a two-tailed test was considered statistically significant.

Results

Baseline patient characteristics

The baseline characteristics of the study population are reported in Table 1. Approximately half of the population was male (n = 24, 43.6%), median age was 45 y (20–75 y) and 76% (n = 42) of patients was diagnosed before the age of 40. According to BMI, the majority of patients had a normal weight (n = 33, 60%), whereas 6 patients (10.9%) were underweight, 12 (21.8%) were overweight, and 4 (7.3%) were clinically obese. Considering patients with CD, mo57.1% had an ileal disease (n = 20), and 48.6% had mainly an inflammatory behavior (n = 17), while left-side colitis was the most prevalent disease location in patients with UC (n = 11, 55%). LFD and SD populations were similar for baseline features, except for a slight preponderance of male sex in patients who were assigned the SD.

Monitoring of disease activity during dietary intervention

After initial assessment (T_0), all patients were randomized, using a computer-generated sequence, to receive either the LFD or SD for a 6-wk period. Accordingly, of the 55 study patients, 26 (47.3%) were assigned to the LFD group, and 29 (52.7%) were assigned to the SD group.

Considering patients with CD, at T_0, 28 (80%) and 7 (20%) were in remission or had mild disease activity, respectively, whereas at T_1, 30 patients (85.7%) were in remission and 5 (14.3%) had mild disease activity ($P = 0.752$). In patients with UC, at T_0, 14 (70%)

Table 1
Main demographic and clinical characteristics of the study cohort

Parameter	All patients (N = 55)	Low-FODMAP diet (n = 26)	Standard diet (n = 29)	*P*-value
Sex (male)	24 (43.6)	7 (26.9)	17 (58.6)	0.04
Age, y	46 (34–57)	41 (34–48)	47 (44–57)	0.11
Age at diagnosis, <40 y	42 (76)	22 (84.6)	20 (69)	0.30
Body mass index, kg/m^2	25.4 (20.3–33.7)	22.2 (15–33.7)	23.3 (18.1–33.2)	0.69
Disease type				0.59
Ulcerative colitis	20 (36.4)	8 (30.8)	12 (41.4)	
Crohn's disease	35 (63.6)	18 (59.2)	17 (48.6)	
CD disease localization				0.69
L1: Terminal ileum	20 (57.1)	11(55)	9 (45)	
L2: Colon	5 (14.3)	3 (60)	2 (40)	
L3: Ileocolon	9 (25.7)	4 (44.4)	5 (55.6)	
L4: Upper GI	1 (2.9)	0 (0)	1 (100)	
CD Behavior				0.08
B1: Non-constricting/Non-penetrating	17 (48.6)	6 (35.3)	11 (64.7)	
B2: Stricturing	10 (28.6)	8 (80)	2 (20)	
B3: Penetrating	8 (22.9)	4 (50)	4 (50)	
UC Localization				0.92
E1: Proctitis	2 (10)	1 (50)	1 (50)	
E: Left-side colitis	11 (55)	4 (36.4)	7 (63.6)	
E3: Pancolitis	7 (5)	3 (42.9)	4 (57.1)	
Smoking status				0.58
Smokers	19 (34.5)	10 (38.5)	9 (31)	
Non-smokers	20 (36.4)	16 (61.5)	20 (69)	
Extraintestinal manifestation	27 (49.1)	13 (50)	14 (48.3)	0.89

CD, Crohn's disease; GI, gastrointestinal; UC, ulcerative colitis.

were in remission and 6 (30%) had mild disease activity, whereas at T_1, 17 patients (85%) were in remission and 3 (15%) had mild disease activity ($P = 0.451$). The proportion of patients in remission at T_0 was similar between those with CD and UC ($P = 0.513$). None of the patients required therapeutic dose adjustment during the 6-wk dietary intervention.

In patients with CD, median HBi value significantly decreased during the study in the whole population ($P = 0.019$). In particular, although there was no statistically significant difference in HBi at T_0 between patients randomized to LFD (4; IQR, 3–5) or SD (3; IQR, 3–3; $P = 0.610$), we found that median HBi significantly decreased in the LFD group (T_1: 3; IQR, 2–3; $P = 0.024$) but not in the SD group (T_1: 3; IQR, 2–4; $P = 0.322$), and that there was no statistically significant difference in HBi between groups at T_1 ($P = 0.283$). In the entire cohort of patients with UC, after the 6-wk dietary intervention, the median Mayo score was unmodified (T_0: 2; IQR, 2–3 versus T_1: 2; IQR, 1–2; $P = 0.275$). When considering the two dietary intervention subgroups, median Mayo scores at T_0 were similar (LFD = 2; IQR, 2–3 versus SD = 2; IQR, 2–3; $P = 0.643$), whereas after the 6-wk dietary intervention they were numerically decreased, although not significantly, in the LFD group (T_1: 1; IQR, 1–3; $P = 0.250$) and they were virtually unmodified in the SD Group (T_1:2; IQR, 1–2; $P = 0.844$), and no difference was observed at this time point between groups ($P = 0.440$).

Biochemical markers of disease activity

Overall, median calprotectin values were significantly higher at baseline (T_0: 88.4 mg/kg; IQR, 50–220.4 mg/kg) compared with median values at the end of the 6-wk dietary intervention (T_1: 55 mg/kg; IQR, 50–125.8 mg/kg; $P = 0.002$; Fig. 2A). There was no statistically significant difference in median calprotectin values at baseline between the LFD group (T_0: 76.6 mg/kg; IQR, 50–286.3 mg/kg) and the SD group (T_0: 91 mg/kg; IQR, 50.6–143.6 mg/kg; $P = 0.741$). However, after the 6-wk dietary intervention, we observed a statistically significant decrease in median calprotectin values in the LFD group (T_1: 50 mg/kg; IQR, 50.6–81 mg/kg; $P = 0.004$; Fig. 2B) but not in the SD group (T_1: 87 mg/kg; IQR, 50–235.6 mg/kg; $P = 0.175$; Fig. 2C), although we observed no statistically significant difference in calprotectin values at T_1 between groups ($P = 0.127$).

Overall, between T_0 and T_1, median calprotectin values decreased by 34.7% and 4.4% in the LFD and SD, respectively.

Lastly, there was no statistically significant difference between median CRP values at T_0 (3.2 mg/L; IQR, 3.1–3.7 mg/L) and at T_1 (3.1 mg/L; IQR, 2–4.9 mg/L; $P = 0.719$) in the entire cohort. There was also no statically significant difference between median baseline CRP values in the LFD group (T_0:3.1 mg/L; IQR, 0.8–3.5 mg/L) and the SD group (T_0: 3.2 mg/L; IQR, 3.1–5 mg/L; $P = 0.341$), and median CRP values were similar at baseline and after the 6-wk dietary intervention in both the LFD group (T_1: 3.1 mg/L; IQR, 2.5–7.6 mg/L; $P = 0.376$) and the SD group (T_1: 3.1 mg/L; IQR, 1.7–4.2 mg/L; $P = 0.159$), and likewise there was no difference between groups at this time point ($P = 0.637$).

Results of dietary intervention on QoL

The median IBD-Q in the whole population at T_0 was 174 (IQR, 143–190), whereas at the end of the 6-wk dietary intervention (T_1) it was 174 (IQR, 155–-190), with no statistically significant difference between the two study time points ($P = 0.742$). The proportion of patients with an IBD-Q >170 at T_0 was 54.5% (n = 30), and it increased to 58.2% (n = 32) at T_1, although this difference was not statistically significant ($P = 0.848$).

At baseline, there was a non-significant trend in lower IBD-Q scores in patients assigned to the LFD group (T_0: 166; IQR, 139–182) compared with patients assigned to the SD group (T_0: 181; IQR, 153–197; $P = 0.06$). After the 6-wk dietary intervention, we observed a modest but statistically significant increase in median IBD-Q in the LFD group (T_1: 177; IQR, 155–188; $P = 0.05$) that was not observed in the SD group (T_1: 166; IQR, 153–200; $P = 0.880$), although the difference between groups at T_1 was not

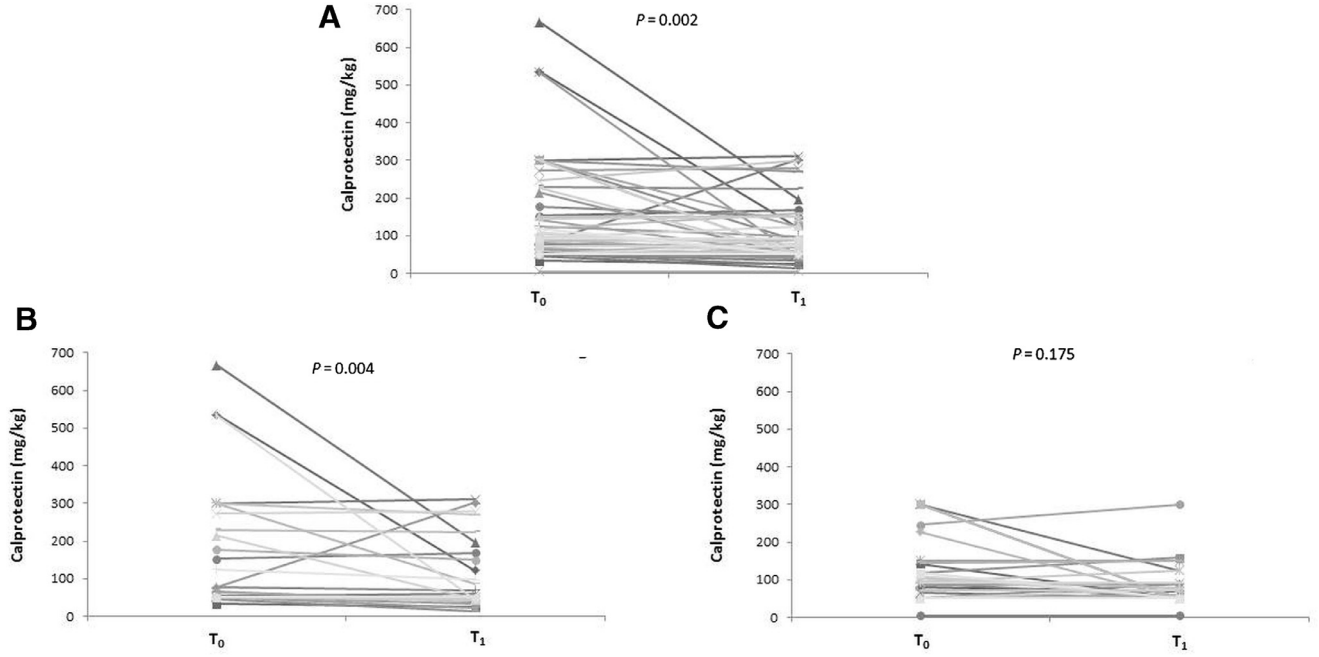

Fig. 2. (**A**) Calprotectin values (mg/kg) at baseline (T_0) and after 6-wk dietary intervention (T_1) in entire cohort. (**B**) Calprotectin values in the low-FODMAP group before (T_0) and after dietary intervention (T_1). (**C**) Calprotectin values in the standard diet group, before (T_0) and after dietary intervention (T_1). FODMAP, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols.

statistically significant ($P = 0.886$). The proportion of patients with an IBD-Q >170 increased from 42.3% (11 of 26 patients) at T_0 to 50% (13 of /26 patients) at T_1 in the LFD group, whereas it remained unchanged in the SD group (65%, 1 of 29 at both T_0 and T_1).

Figure 3 shows the various subcategories of the IBD-Q scores at baseline and at the end of the 6-wk dietary intervention: Overall, we observed no significant modification in the various IBD-Q subcategories in either study group.

Discussion

Symptoms compatible with a diagnosis of IBS are highly prevalent in the general population, as 11% of individuals worldwide are reportedly affected by this condition, although with both demographic and geographic variations [26,27]. Patients with IBD reportedly have an even higher prevalence of symptoms that are suggestive of IBS such as bloating, diarrhea, and abdominal pain and these symptoms are reported by 57% of patients with CD and 33% of patients with UC [6,8]. Noteworthy, these symptoms frequently occur in patients with quiescent IBD or in those with minimal disease activity, and may profoundly impair patients QoL as well as trigger an unnecessary treatment escalation [7,9].

The use of an LFD has been suggested as a potential therapeutic aid for these patients due to its good results in patients with IBS as well as in other intestinal conditions [15,28–31]. In 2009, a pilot study assessed the role of an LFD on intestinal symptoms in patients with IBD and found an improvement in bowel symptoms, although the study was carried out via telephone interviews, there was no control group and no monitoring of IBD activity; a similar study, carried out retrospectively reviewing case notes of electronic medical records, described a positive outcome in terms of global reduction in intestinal symptoms and stool frequency with an LFD, although also in this study there was no formal assessment of IBD activity [16,17]. More recently, a randomized, double-blind, placebo-controlled, crossover, rechallenge study carried out in a small series of patients with IBD found that mainly fructans exacerbated intestinal symptoms in patients with IBD, and despite the very low number of patients with available data (n = 24), fecal calprotectin levels were higher at the end of the trial, especially in CD patients, thus emphasizing the need for further studies to assess the safety of the LFD diet in patients with IBD [18]. In this regard, it is hypothesized that FODMAPs, through their prebiotic effect on colonic bacteria, may have indirect immunomodulating properties, and their withdrawal might therefore exert a detrimental effect on intestinal inflammation [32].

The aim of this prospective study was to evaluate the effect of an LFD on intestinal markers of inflammation, disease activity, and QoL in patients with quiescent or minimal activity IBD who were in stable clinical conditions for >3 mo. During the study, patients were clinically monitored, and both fecal calprotectin values and CRP levels were assessed at baseline and after the 6-wk dietary intervention to identify possible disease exacerbations as well as modifications in subclinical intestinal inflammation.

We observed that, after the dietary intervention, the proportion of patients with quiescent disease increased, although not significantly, from 76.4% at baseline to 85.4% at the end of the study; moreover, we found that, in the short term, the LFD is associated with a statistically significant decrease in HBi in patients with CD and a numerically decrease in Mayo score in those with UC, respectively. It should be emphasized that an overlap with IBS is often present in patients with IBD during disease remission phases. In a recent study, Testa et al. observed that the LFD may represent a

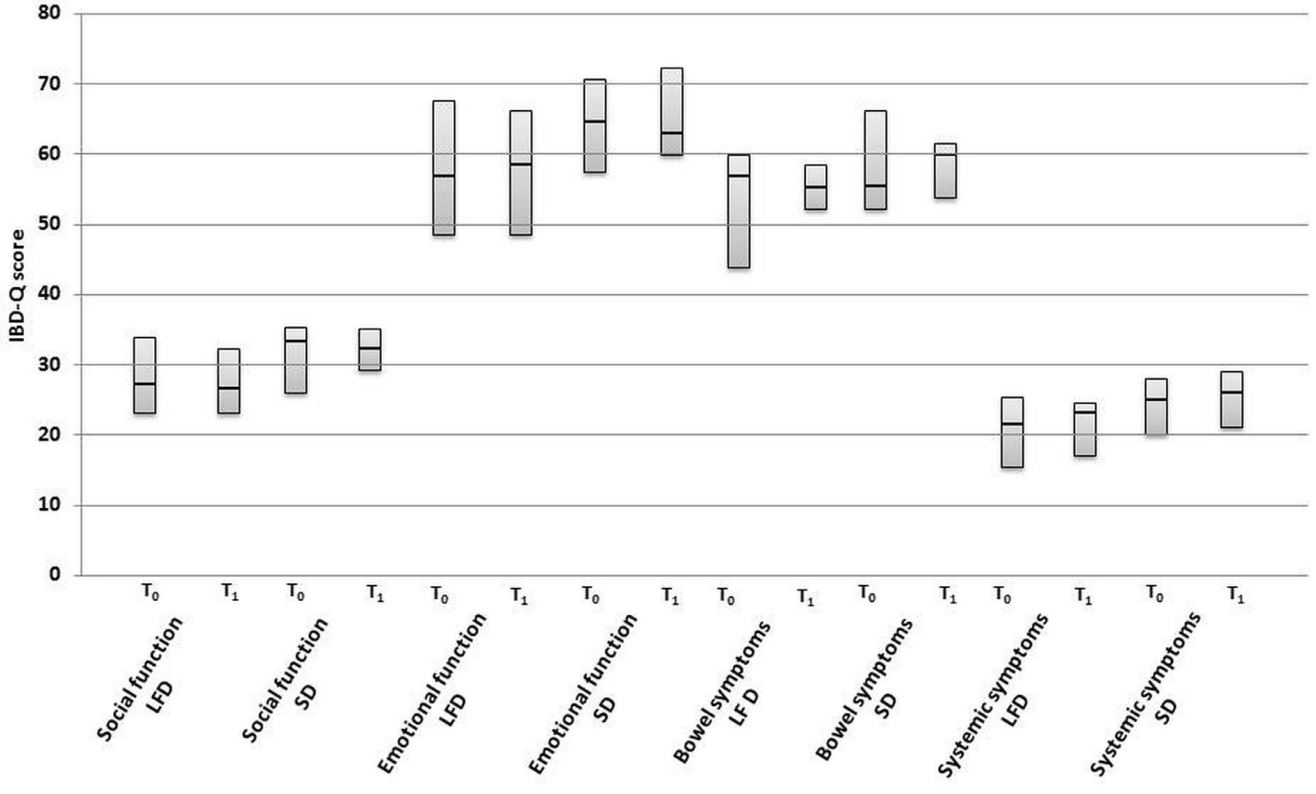

Fig. 3. Median (solid line) and interquartile range (gray box areas) of the various IBD-Q items in patients randomized to the LFD and to the SD at baseline (T_0) and after the 6-wk dietary intervention (T_1). IBD-Q, Inflammatory Bowel Disease Questionnaire; LFD, low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols diet; SD, standard diet.

valid option so as to improve bowel symptoms in patients with quiescent IBD and concomitant IBS, thus leading to an amelioration of patient QoL life [33]. It is noteworthy that IBD activity scores were already in the low range at baseline, as per inclusion criteria, and therefore this further decrease in patients who were in stable conditions for >3 mo is of particular note.

Although we observed that, after dietary intervention, median CRP levels were virtually unmodified in the entire cohort as well as in the two study subgroups, a finding mainly related to the inclusion of patients with stable, quiescent disease in more than two-thirds of the population. Fecal calprotectin values significantly decreased in the entire cohort, and this result was mainly due to their significant reduction in patients assigned to the LFD. However, we must also emphasize the fact that median calprotectin values at baseline were similar in the LFD and SD groups. Considering bowel inflammation in patients with IBD, fecal calprotectin is considered a more specific laboratory parameter than CRP to assess intestinal inflammation. However, despite the fact that the LFD may have an indirect effect on gut microbiota due to a restriction in fructans and galacto-oligosaccharides, which are dietary prebiotics, the patients included in the study were in remission or had mild disease activity, and therefore the observed decrease in fecal calprotectin at the end of the study should be conservatively interpreted as a lack of potential worsening of disease secondary to the dietary intervention. The potential explanations for a reduction in fecal calprotectin remain inconclusive, and we believe that the effects of the LFD on gut microbiota and inflammation require further investigation.

Finally, we observed a slight, barely significant improvement in global IBD-Q scores in patients assigned to the LFD and no modification of IBD-Q in patients who followed the SD. Patients assigned to the SD already had fairly higher IBD-Q scores at baseline, and although no improvement was observed in the proportion of patients with a satisfactory IBD-Q result in this group (65% both at baseline and at the of the dietary intervention), the proportion of patients with an IBD-Q >170 increased, from 42.3% to 50%, in patients assigned to the LFD.

Some studies hypothesized that the LFD may be detrimental for patients affected by IBD. A previous study found that fecal calprotectin was higher at the end of the diet trial in patients with CD, and although the authors could not draw a definite conclusion, the literature reports that the LFD may indirectly modulate immune gut functions, and dietary restrictions may negatively affect the gut microbiota [17,18]. On the other hand, in this regard, another study carried out in a very small cohort of eight patients with CD for a short period of time (i.e., 3 wk) found that the LFD had no influence of fecal calprotectin levels, although increasing the FODMAP diet content had a consistent prebiotic effect with a consequent worsening of intestinal symptoms, and it has also been hypothesized that increasing amounts of FODMAP may be associated with the development of CD [34,35].

This study had some limitations. We did not evaluate endoscopic disease activity, but we deemed it unethical to perform endoscopy within 6 wk of diet intervention in patients with no clinically meaningful change in disease status; moreover, we observed that, after adequate explanation of the LFD, ~3% of the initial cohort preferred not being enrolled into the study, and therefore the potential, wider clinical application of this dietary approach also may be influenced by patient preference. Finally, the study period was limited to six weeks and the cohort enrolled in this pilot study was small, thus were are unable to predict potential positive and negative reflexes of the LFD during longer periods of time.

Conclusion

We found that a short-term LFD is associated with an amelioration of fecal biomarkers of intestinal inflammation in patients with IBD, and reduced disease activity in patients with CD, even in patients with mainly quiescent disease, and that this dietary intervention seems to improve, albeit slightly, patient QoL. These positive and encouraging results should be confirmed in larger series.

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